

CLAIM LISTING

1. (Currently Amended) A method of monitoring polymer array synthesis on a solid substrate comprising:

(i) synthesizing a preselected array of diverse biological polymers connected to ~~cleavable linkers on~~ a solid substrate, whereby the diverse biological polymers occupy different regions of the substrate and are spatially defined on the solid substrate on which the preselected array is synthesized, and wherein the diverse biological polymers comprise nucleotides, nucleosides, phosphoramidites, carbohydrates or natural or synthetic amino acids;

(ii) cleaving the diverse biological polymers from the solid substrate by ~~cleaving the cleavable linkers~~, thereby creating a mixture of diverse unbound biological polymers; and

(iii) predicting a quantity of diverse biological polymers formed and comparing a measurement of quantity of diverse cleaved biological polymers from the array with the predicted quantity of diverse biological polymers formed as an indicator of the efficiency of the synthesis procedure, thereby determining the efficiency of the synthesis procedure.

2. (Previously Presented) The method of claim 39, wherein each of the labeled polymers comprises a single isomeric label.

3. (Previously Presented) The method of claim 39, wherein the labeled unbound polymers are heterogeneous by number of monomeric units, and wherein the method further comprises separating the labeled unbound polymers by number of monomeric units.

4. (Previously Presented) The method of claim 39, wherein the labeled unbound polymers are heterogeneous by number of monomeric units, and wherein the method further comprises separating the labeled unbound polymers by charge using ion exchange chromatography.

5. (Previously Presented) The method of claim 39, wherein each of the labeled unbound polymers are heterogeneous by number of monomeric units, and wherein the method further comprises separating the labeled unbound polymers by number of monomeric units using capillary gel electrophoresis.

6. (Original) The method of claim 4, wherein the ion exchange chromatography is performed by HPLC.

7. (Original) The method of claim 4, wherein the ion exchange chromatography is performed by HPLC, and wherein the labeled unbound polymers are detected as they exit an ion exchange column.

8. (Original) The method of claim 1, wherein the polymer is an oligonucleotide.

9. (Cancelled)

10. (Previously Presented) A method for measuring the effect of altering a polymer array synthesis protocol, comprising:

(i) synthesizing a preselected array of diverse biological polymers occupying different regions on a solid support by a first synthesis protocol, wherein the diverse biological polymers are spatially defined on the solid support on which the preselected array is synthesized, thereby creating a reference array of biological polymers, wherein the diverse biological polymers comprise nucleotides, nucleosides, phosphoramidites, carbohydrates or natural or synthetic amino acids;

(ii) synthesizing a preselected array of diverse biological polymers occupying different regions on a solid support synthesized by a second synthesis protocol, wherein the diverse biological polymers are spatially defined on the solid support on which the preselected array is synthesized, and wherein the second synthesis protocol is different than the first synthesis protocol, thereby creating a test array of biological polymers; wherein biological polymers of the test array are preselected to be the same as preselected biological polymers of the reference array;

(iii) cleaving separately the reference array of biological polymers and the test array of biological polymers, thereby creating a mixture of diverse cleaved biological polymers from the reference array and a mixture of diverse cleaved biological polymers from the test array;

(iv) comparing a measurement of presence of diverse cleaved biological polymers from the test array as an indicator of the efficiency of the second synthesis procedure

with a measurement of presence of diverse cleaved biological polymers from the reference array as an indicator of the efficiency of the first synthesis procedure, thereby determining whether a difference between the first and second synthesis procedure affects the efficiency of the second synthesis procedure.

11. (Original) The method of claim 10, wherein the test and reference polymers are oligonucleotides.

12. (Original) The method of claim 10, wherein the first synthesis protocol differs from the second synthesis protocol by a single variation.

13. (Original) The method of claim 10, wherein the reference polymers and the test polymers are attached to the solid substrate by a cleavable linker.

14. (Original) The method of claim 10, wherein the test and reference polymers comprise a detectable label.

15. (Previously Presented) The method of claim 14, wherein the label is a single isomeric label.

Claims 16-36: (Cancelled)

37. (Previously Presented) The method of claim 39, wherein the labeled polymers comprise a label comprising a fluorescent moiety.

38. (Previously Presented) The method of claim 14, wherein the detectable label comprises a fluorescent moiety.

39. (Previously Presented) The method of claim 1, wherein each of the polymers further comprises a label, thereby forming labeled polymers.

40. (Currently Amended) A method of monitoring polymer array synthesis on a solid substrate comprising:

(i) synthesizing a preselected array of diverse polymers ~~connected to cleavable linkers~~ on a solid substrate, whereby the diverse polymers occupy different regions of the solid substrate and are spatially defined on the solid substrate on which the preselected array is synthesized;

(ii) cleaving the diverse polymers from the solid substrate ~~by cleaving the cleavable linkers~~; thereby creating a mixture of diverse unbound polymers; and

(iii) predicting a quantity of diverse polymers formed and comparing a measurement of quantity of diverse cleaved polymers from the array with the predicted quantity of diverse polymers formed as an indicator of the efficiency of the synthesis procedure, thereby determining the efficiency of the synthesis procedure.

41. (Previously Presented) The method of claim 40, wherein each of the polymers further comprises a label, thereby forming labeled polymers.

42. (Previously Presented) The method of claim 41, wherein the labeled polymers comprise a label comprising a fluorescent moiety.

43. (Previously Presented) The method of claim 41, wherein each of the labeled polymers comprises a single isomeric label.

44. (Previously Presented) The method of claim 41, wherein the labeled unbound polymers are heterogeneous by number of monomeric units, and wherein the method further comprises separating the labeled unbound polymers by number of monomeric units.

45. (Previously Presented) The method of claim 41, wherein the labeled unbound polymers are heterogeneous by number of monomeric units, and wherein the method further comprises separating the labeled unbound polymers by charge using ion exchange chromatography.

46. (Previously Presented) The method of claim 41, wherein each of the labeled unbound polymers is heterogeneous by number of monomeric units, and wherein the method further comprises separating the labeled unbound polymers by number of monomeric units using capillary gel electrophoresis.

47. (Previously Presented) The method of claim 45, wherein the ion exchange chromatography is performed by HPLC.

48. (Previously Presented) The method of claim 45, wherein the ion exchange chromatography is performed by HPLC, and wherein the labeled unbound polymers are detected as they exit an ion exchange column.

49. (Previously Presented) The method of claim 40, wherein the polymer is an oligonucleotide.

50. (Previously Presented) A method for measuring the effect of altering a polymer array synthesis protocol, comprising:

(i) synthesizing a preselected array of diverse polymers occupying different regions on a solid support by a first synthesis protocol, wherein the diverse polymers are spatially defined on the solid support on which the preselected array is synthesized, thereby creating a reference array of polymers;

(ii) synthesizing a preselected array of diverse polymers occupying different regions on a solid support synthesized by a second synthesis protocol, wherein the diverse polymers are spatially defined on the solid support on which the preselected array is synthesized, and wherein the second synthesis protocol is different than the first synthesis protocol, thereby creating a test array of polymers;

(iii) cleaving separately the reference array of polymers and the test array of polymers, thereby creating a mixture of diverse cleaved polymers from the reference array and a mixture of diverse cleaved polymers from the test array;

(iv) comparing a measurement of presence of diverse cleaved polymers from the test array as an indicator of the efficiency of the second synthesis procedure with a measurement of presence of the mixture of diverse cleaved polymers from the reference array as

an indicator of the efficiency of the first synthesis procedure, thereby determining whether a difference between the first and second synthesis procedures affects the efficiency of the second synthesis procedure.

51. (Previously Presented) The method of claim 50, wherein the test and reference polymers are oligonucleotides.

52. (Previously Presented) The method of claim 50, wherein the first synthesis protocol differs from the second synthesis protocol by a single variation.

53. (Previously Presented) The method of claim 50, wherein the reference polymers and the test polymers are attached to the solid substrate by a cleavable linker.

54. (Previously Presented) The method of claim 50, wherein the test and reference polymers comprise a detectable label.

55. (Previously Presented) The method of claim 54, wherein the label is a single isomeric label.

56. (Previously Presented) The method of claim 54, wherein the detectable label comprises a fluorescent moiety.

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